Approved for use through 10-31-99. OMB 0651-0031
Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork	Reduction /	Act of 1995	no perso	ns are requ	ired to respo	nd to a collection of in	ormation unless it co	ontains a valid OMB cont	rol number.	
Substitute for fo	orm 1449	A/PTO				COMPLET	E IF KNOWN			
INFORMA	TION	DISC	LOS	URE		Application	Number	10/815,198		
STATEME	ENT B	Y APP	LICA	NT	٠	Filing Date		March 25, 200)4	
I.P.E (USA)	s many she	ets as nec	essary)			First Named	Inventor	PALMISANC	et al	
19200 6			•			Group Art U	nit	1645 1645	3	
	1					Examiner N	ame	Hama M	M. Harris, Ph.D.	
& TS hoomen Ry	1		of	5		Attorney Do	cket Number	41543 US 010		
U.S. PATENT	DOCUM	IENTS								
Examiner Initials	Cite No.1	. <u>U</u> Number	Kind	t Docume Code 2 (if know		Name of Pa Applicant Docum	of Cited	Date of Publication of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	
and		6,017,	704	Α		Herman, et al.		01/25/2000		
anh		5,786,	146	Α		Herman, et al.		07/28/1998		

							•		·	
			•		·					
FOREIGN PA	TENT D	OCUME	ENTS			<u> </u>		<u> </u>		
Examiner Initials	Cite No.	T	oreign P		Kind Kind Code f known)	Name of Pa Applicant Docur	of Cited	Date of Publication of Cited Document	Pages, Columns, Lines Where Relevant Passages or Relevant Figures Appear	Т 6
Examiner Signature		a	mt	ar	ùs	· · · · · · · · · · · · · · · · · · ·	Date Considered	30 Du	24 2009	

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[G:\ANNETTE\LRRI-BelinskyPAX5_1449p1.PTO.doc]

^{1.} Unique citation designation number. 2. See attached Kinds of U.S. Patent Documents. 3. Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). 4. For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. 5. Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. 6. Applicant is to place a check mark here if English language Translation is attached.

Please type a	plus sign	(+) inside	this box
---------------	-----------	------------	----------

П
ויו

PTO/SB/08B (10-96)
Approved for use through 10-31-99. OMB 0651-003
Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number. COMPLETE IF KNOWN Substitute for form 1449B/PTO **Application Number** 10/815,198 INFORMATION DISCLOSURE Filing Date March 25, 2004 STATEMENT BY APPLICANT First Named Inventor PALMISANO et al (use as many sheets as necessary) Group Art Unit A.M. Harris, Ph.D. **Examiner Name** 5 Attorney Docket Number Sheet of 41543 US 0103

Examiner Initials	Cite No. 1	Include name of the author (in CAPITAL LETTERS), title of article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	T²
amh		ANTEGUERA, F., et al., "CpG Islands," DNA Methylation: Molecular Biology and Biological Significance, Ed by J.P. Jost & H.P Saluz, Birkhauser Verag Basel/Switzerland, Vol. 64 pp 169-185 1993	
amh		BAYLIN, S.B., et al., "DNA Hypermethylation in Tumorigenesis," <i>Trends in Genetics</i> , Vol. 16 pp 168-174, 2000	
amh		BELINSKY, S.A., et al., "Aberrant Methylation of p16 ^{INK4a} is an Early Event in Lung Cancer and a Potential Biomarker for Early Diagnosis," <i>Proc. Natl. Acad. Sci USA</i> , Vol. 95, pp 11191-11896 Sep 1998	
anh		BROCK, G.J.R., et al., "A Novel Technique for the Identification of CpG Islands Exhibiting Altered Methylation Patterns (ICEAMP)", Nucleic Acids Research, Vol. 29, No. 24e 2001	
anh		BURBEE, D.G., et al., "Epigenetic Inactivation of RASSSF1A in Lung and Breast Cancers and Malignant Phenotype Suppression," <i>J of Natl Canc Inst</i> , Vol. 93, No. 9, pp 691-699 2001	
		BUSSLINGER, M., et al., "Deregulation of PAX-5 by Translocation of the Eµ Enhancer of the IgH Locus Adjacent to Two Alternative PAX-5 Promoters in a Diffuse Large-cell Lymphoma," Proc. Natl. Acad. Sci USA, Vol. 93, pp 6129-6134 June 1996	
/		CARTER, M.G., et al., "Mice Deficient in the Candidate Tumor Suppressor Gene Hicl Exhibit Development Defects of Structures Affected in the Miller-Dieker Syndrome," Human Molecular Genetics, Vol. 9, No. 3, pp 413-419 2000	
V		DU, Y., et al., "Hypermethylation in Human Cancers of the RIZI Tumor Suppressor Gene, a Member of a Histone/Protein Methyltransferase Superfamily," Cancer Research, Vol. 61, pp 8094-8099 Nov 15 2001	

Examiner Signature	amta	tous	Date Considered	08/20/2027	

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[G:\ANNETTE\LRRI-BelinskyPAX5_1449p2.PTO.doc]

Unique citation designation number. 2. Applicant is to place a check mark here if English language Translation is attached.

	_	
	1.1	
- 1		
- 1	'1	

PTO/SB/08B (10-96)
Approved for use through 10-31-99. OMB 0651-003
Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Pap	erwork R	eduction Act o	f 1995, no per	sons are required to respond to a collection of i	information unless it contains a valid OMB control number.
Substitu	te for f	form 1449	B/PTO	COMPLETE IF KNOWN	
INEOD	N/ A T	יות וארטי	B/PTO CLOSURE PLICANT cessary)	Application Number	10/815,198
	NFORMATION DISCLOSURE TATEMENT BY APPLICANT (use as many sheets as necessary)	Filing Date	March 25, 2004		
	•			First Named Inventor	PALMISANO et al
(1	ise as mai	ny sheets as ne	cessary)	Group Art Unit	1643
				Examiner Name	A.M. Harris
Sheet	3	of	5	Attorney Docket Number	41543 US 0103

OTHER PRI	OR ART -	NON PATENT LITERATURE DOCUMENTS	
Examiner Initials	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	T²
anh		COSTELLO, J.R., et al., "Aberrant CpG-Island Methylation has Non-Random and Tumour-type-specific Patterns," <i>Nature Genetics</i> , Vol. 25, pp 132-138 Feb 2000	
anti		ESTELLER, M., et al., "A Gene Hypermethylation Profile of Human Cancer," Cancer Research, Vol. 61, pp 3225-3229 Apr 15 2001	
amh		ESTELLER, M., et al., "Detection of Aberrant Promoter Hypermethylation of Tumor Suppressor Genes in Serus DNA from Non-Small Cell Lung Cancer Patients," Cancer Research, Vol. 59, pp 67-70 Jan 1 1999	
amh		ESTELLER, M., et al., "Inactivation of the DNA Repair Gene O ⁶ -Methylguanine-DNA Methytransferase by Promoter Hypermethylation is a Common Event in Primary Human Neoplasia," Cancer Research, Vol. 59, pp 793-797 Feb 15 1999	
anh		GARDINER-GARDEN, M., et al., "CpG Islands in Vertegrate Genomes," J. Mol. Biol., Vol. 196, pp 261-282 1987	
		GONZALGO, M.L., et al., "Identification and Characterization of Differentially Methylated Regions of Genomic DNA by Methylation-sensitive Arbitrarily Primed PCR," Cancer Research, Vol.57, pp 5940599 Feb 15 1997	
V		HUANG, T.H-M, et al., "Identification of DNA Methylation Markers for Human Breast Carcinomas Using for Methylation-Sensitive Restriction Fingerprinting Technique," Cancer Research, Vol. 57 pp 1030-1034 Mar 15 1997	
ant		ISSA, J-P J., et al., "H1C1 Hypermethylation is a Late Event in Hematopoietic Neoplasms," Cancer Research, Vol. 57 pp 1678-1681 May 1 1997	

	A		
Examiner Signature	antaris	Date Considered	30 July 2007

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[G:\ANNETTE\LRRI-BelinskyPAX5_1449p3.PTO.doc]

Unique citation designation number. 2. Applicant is to place a check mark here if English language Translation is attached.

_	
ы	
т	

PTO/SB/08B (10-96)
Approved for use through 10-31-99, OMB 0651-003
Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no

persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitut	te for f	orm 1449	B/PTO	COMPLETE IF KNOWN	
INEOD	N // A T	ION DI	SCLOSURE	Application Number	10/815,198
			PPLICANT	Filing Date	March 25, 2004
				First Named Inventor	PALMISANO et al
(t	ise as mai	ny sheets as ne	cessary)	Group Art Unit	1645-1643
				Examiner Name	A.M. Harris, Ph.D.
Sheet	4	of	5	Attorney Docket Number	41543 US 0103

Examiner Initials	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	T ²
amh		JOHNSON, D.H., et al., "Recent Advances with Chmotherapy for NSCLC: The ECOG Experience," Oncology, Vol. 12, No. 1, Suppl 2 pp 67-70 Jan 1998	
amh		JONES, P.A., et al., "Cancer Epigenetics Comes of Age," <i>Nature Genetics</i> , Vol. 21 pp 163-167 Feb 1999	
\int		PALMISANO, W.A., et al., "Aberrant Promoter Methylation of the Transcription Factor Genes PAX5 α and β in Human Cancers," Cancer Research Vol. 63 pp 4620-4625 Aug 1 2003	
		PALMISANO, W.A., et al., "Predicting Lung Cancer by Detecting Aberrant Promoter Methylation in Sputum," Cancer Research Vol. 60 pp5954-5958 Nov 1 2000	
,		SALEM, C.E., et al., "PAX6 Methylation and Ectopic Expression in Human Tumor Cells," Int. J. Cancer Vol 87 pp 179-185 2000	
V.		SCHÄFER, B.W., "Emerging Roles for PAX Transcription Factors in Cancer Biology," Gen. Physiol. Biophys Vol 17 pp 211-224 1998	
amh		SILVA, J.M., et al., "Persistence of Tumor DNA in Plasma of Breast Cancer Patients After Mastectomy," Annals of Surgical Oncology Vol 9, No. 1 pp 71-76 2002	,
ann		STUART E.T., et al., "Loss of p53 Function Through PAX-Mediated Transcriptional Repression," <i>The EMBO Journal</i> Vol. 14, No. 22 pp 5638-5645 1995	
amh		STUART, E.T., et al., "PAX and HOX IN Neoplasia," Advances in Genetics Vol 33 pp 255-275 1995	

Examiner Signature	amfarris	Date Considered	30 July 2007	
-----------------------	----------	--------------------	--------------	--

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[G:\ANNETTE\LRRI-BelinskyPAX5_1449p4.PTO.doc]

Unique citation designation number. 2. Applicant is to place a check mark here if English language Translation is attached.

+	

PTO/SB/08B (10-96)
Approved for use through 10-31-99. OMB 0651-003
Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Par	perwork R	eduction Act	of 1995, no pers	ons are required to respond to a collection of in	nformation unless it contains a valid OMB control number.
Substitute for form 1449B/PTO				COMPLETE IF KNOWN	
INFOR	MAT	ות אסו־	SCLOSURE	Application Number	10/815,198
INFORMATION DISCLOSURE STATEMENT BY APPLICANT				Filing Date	March 25, 2004
				First Named Inventor	PALMISANO et al
,,	(use as many sheets as necessary)			Group Art Unit	1045 1643
				Examiner Name	A.M. Harris, Ph.D.
Sheet	5	of	5	Attorney Docket Number	41543 US 0103

Examiner	Cite	Include name of the author (in CAPITAL LETTERS), title of article (when appropriate), title of	Ī	
Initials	No. '	the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published		
auch		TESTA, J.R., et al., "Cytogenic Analysis of 63 Non-Small Cell Lung Carcinomas: Recurrent Chromosome Alterations Amid Frequent and Widespread Genomic Upheaval," Genes, Chromosomes & Cancer, Vol. 11 pp 178-194 1994		
amh		TOYOOKA, K.O., et al., "Loss of Expression and Aberrant Methylation of the CDH13 (H-Cadherin) Gene in Breast and Lung Carcinomas," Cancer Research Vol 61 pp 4556-4560 June 1 2001	T	
anh		TOYOTA, M., et al., "Identification of Differentially Methylated Sequences in Colorectal Cancer by Methylated CpG Island Amplification," Cancer Research Vol. 59 pp 2307-2312 May 15 1999		
(.		TOYOTA, M., et al., "CpG Island Methylator Phenotype in Colorectal Cancer," Proc. Natl Acad Sci USA Vol 96 pp 8681-8686 July 1999		
V		TOYOTA, M., et al., "Inactivation of CACNAIG, A t-Type Calcium Cannel Gene, by Aberrant Methylation of its 5' CpG Island in Human Tumors," Cancer Research Vol 59 pp 4535-4541 Sep 1 1999		
anh		WALES, M.M., et al., "p53 Activates Expression of HIC-1, A New Candidate Tumour Supressor Gene on 17p13.3," Nature Medicine, Vol 1 No 6 pp570-577 June 1995		
and		YAN, P.S., et al., "Dissecting Complex Epigenetic Alterations in Breast Cancer Using CpG Island Microarrays," Cancer Research Vol 61 pp 8375-8380 Dec 1 2001		
		YANG, X., et al., "DNA Methylation in Breast Cancer," Endocrin-Related Cancer, Vol. 8, pp 115-127 2001		
V		ZÖCHBAUER-MÜLLER, S., et al., "5' CpG Island Methylation of the <i>fhit</i> Gene is Correlated with Loss of Gene Expression in Lung and Breast Cancer," Cancer Research Vol 61, pp 3581-3585 May 1 2001		
anh		ZOU, H-Z, et al., "Detection of Aberrant p16 Methylation in the Serum of Colorectal Cancer Patients," Clinical Cancer Res, Vol. 8, pp 188-191 Jan 2002		
Examiner Signature		MM Hours Date Considered 08/20/2087		

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[G:\ANNETTE\LRRI-BelinskyPAX5_1449p5.PTO.doc]

Unique citation designation number. 2. Applicant is to place a check mark here if English language Translation is attached.

Unknown A. M. Harris, Ph.D.

US PATENT DOCUMENTS					
Examiner Cite USP Document Publication Name of Patentee or Applicant of cited Document Filing Date Initial * No Number Date					

Attorney Docket No: 41543 US 0103

Examiner Name

FOREIGN PATENT DOCUMENTS					
Examiner Initials*	Foreign Document No	Publication Date	Name of Patentee or Applicant of cited Document	T²	
ûm	WO 02/068694 A1	09/06/2002	Johns Hopkins Univ School/Goggin,		

	OTHE	R DOCUMENTS NON PATENT LITERATURE DOCUMENTS	
Examiner Initials*	Cite No ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T³
anh		CHIUBACHI, T., et al., "Hypermethylation of the Human PAX-5 Gene Promoter", 41st Annual Meeting of Amer Soc of Hematology, New Orleans LA USA (Dec 3-7 1999), Vol. 94, No. 10, Suppl 1 part 2, (11/15/1999),296b	

Filed December 29, 2005

G:\ANNETTE\LRRI-Belinsky_198_1449.PTO.doc

(Use as many sheets as necessary)

Sheet

EXAMINER OMHUUS

DATE CONSIDERED 08/28/2007

Approved for use through 10-31-99. OMB 0651-0031
Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995 no persons are required to respond to a collection of information unless it contains a valid OMB control number. Substitute for form 1449A/PTO COMPLETE IF KNOWN 819,198 Application Number INFORMATION DISCLOSURE STATEMENT BY APPLICANT Filing Date March 25, 2004 First Named Inventor Palmisano (use as many sheets as necessary). 1643 Group Art Unit A.M. Harris, Ph.D. **Examiner Name** 2 1 of Sheet Attorney Docket Number 41543 US 0103 **U.S. PATENT DOCUMENTS** Cite Examiner U.S. Patent Document Name of Patentee or Date of Pages, Columns, Lines, Initials No.1 Applicant of Cited Kind Code 2 Publication Where Relevant Document of Cited Passages or Relevant (if known) Number Document Figures Appear FOREIGN PATENT DOCUMENTS Examiner Cite Foreign Patent Document Name of Patentee or Date of Pages, Columns, Lines Initials No. Applicant of Cited Publication Where Relevant Code 5 Document of Cited Passages or Relevant Office Number Document Figures Appear Т (if known) WO99/63110 PCT ΑI Imperial College Innov. Ltd 09.12.1999 Examiner Date Signature Considered

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[G:\ANNETTE\LRRI-Belinsky-1449p1.PTO.doc]

^{1.} Unique citation designation number. 2. See attached Kinds of U.S. Patent Documents. 3. Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). 4. For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. 5. Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. 6. Applicant is to place a check mark here if English language Translation is attached.

_
-4

Approved for use through 10-31-99. OMB 0651-003

Substitute for form 1449B/PTO		COMPLETE IF KNOWN	``		
INFOR	M A T	יות אחני	SCI OSIIDE	Application Number	10/815,198
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (use as many sheets as necessary)				Filing Date	March 25, 2004
			•	First Named Inventor	Palmisano
			cessary)	Group Art Unit	1643
				Examiner Name	A.M. Harris
Sheet	2	of	2	Attorney Docket Number	41543 US 0103

2001)
1

Examiner Signature	authoris	Date Considered	36 July 2007
EVAMINED. Initial	1:66		

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[G:\ANNETTE\LRRI-Belinsky-1449p2.PTO.doc]

Unique citation designation number. 2. Applicant is to place a check mark here if English language Translation is attached.